## REMARKS

Claims 1-30 are pending.

The Examiner in the prior application Serial No. 09/731,657 relied on Brenner v. Manson 148 USPQ 689 (S Ct 1966) to assert certain of the claims were not patetable under 35 U.S.C. §101. As explained in the prior application prosecution, the applicants believe the Examiner's reliance on Brenner is misplaced as the Patent Office has previously acknowledged that Brenner dealt with the rare situation where "an applicant fails entirely to indicate why the claimed invention is useful." See, fn, 4, page 16 of "Legal Analysis Supporting Utility Examination Guidelines", Department of Commerce, Patent and Trademark Office, Docket No. 950706162-5172-01 executed July 3, 1995, by Bruce A. Lehman, Assistant Secretary of Commerce and Commissioner of Patents and Trademarks (copy attached)[1].

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[1] The applicants reliance on the following legal analysis of the Patent Office is appropriate. The prior Examiner indicated on page 2 of the Office Action dated March 24, 2003 (Paper No. 14) of the prior application Serial No. 09/731,657 that the applicants have "completely ignore[d] the subsequent "REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS" (http://ptoweb.uspto.gov/patents/filecab/documents/utility.pdf-188.OKB, 28 Feb. 2000) upon which the instant [§101] rejection [of claims 1 to 5, 17, 21 and 22] is based and which the Applicant is encouraged to review. Applicant has failed to identify any inconsistency between those subsequent guidelines and the instant rejection."

As a procedural matter, the undersigned notes that the web site and contents thereof noted by the Examiner was not accessible to the undersigned. The Examiner is requested to supply a paper copy of any document relied upon in making a rejection so that the record may be clear and the applicants are afforded an ample opportunity to consider all of the Examiner's reasoning.

A copy of a document titled "Revised Interim Utility Guidelines Training Materials (1999) (PDF)" was obtained by the undersigned from http://www.uspto.gov/web/patents/guides.htm and a copy of the same is attached for completeness. The Examiner is requested to confirm that the attached are the Guidelines referenced to by the Examiner in the noted Paper No. 14.

As a substantive matter, the applicants note that their previous and present comments relate to the Patent Office Legal Analysis Supporting Utility Examination Guidelines, as noted above. The applicants have not argued that the Examiner has not followed Patent Office guidelines or training materials so to do so would be contrary to the Patent Office regular reminder that Patent Office guidelines and training materials are not intended to, nor do they have, the force or effect of law. See, attached 60 FR 36263, right column, last paragraph.

The Patent Office has recognized that Brenner required an applicant to disclose a utility in his application. Specifically, the Patent Office has noted

> "Courts have found an application deficient under the "usefulness" portion of § 101 where the applicant has not identified any "specific" utility for the invention. Such situations arise rarely; namely where an applicant fails entirely to indicate why the claimed invention is useful. For example, in Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966), the Supreme Court affirmed a finding by the Office that a method of producing a particular class of steroids was deficient under § 101 because the applicant did not explain why the compounds produced by the claimed process were useful. The process in question was patented by another who had disclosed a utility for the invention. The Court refused to consider sufficient a general assertion, not made in the application as filed but instead made by the applicant during an interference proceeding, that the compounds in question were structurally similar to others and therefore might possess a particular biological activity in common with those other compounds. Thus, the Court focused on the fact that the applicant failed to identify any "specific utility" for the claimed invention in his application. A more recent case involved an assertion that a disclosure that a substance was "plastic-like" and could be pressed into films was insufficient to satisfy § 101. In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993). As the court stated:

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The Examiner is correct that the Guidelines published at 60 FR 36263 – 36265 (copy attached) were superseded by the Guidelines ("Revised Utility Examination Guidelines; Request for Comments") published at 64 FR 71440 (December 21, 1999) (copy attached) which were finally published as new Guidelines ("Utility Examination Guidelines") at 66 FR 1092-1099 (copy attached). While the attached series of Guidelines evolved from the Guidelines published in 1995 (copy attached), the Legal Analysis which is described in 60 FR 36265 (July 14, 1995), and a copy of which is attached, is not mentioned in subsequent Guidelines as having been revised. See, 60 FR 36265 (middle column "Additional Information") (copy attached). Accordingly, the applicants submit, with all due respect, that the previously indicated and following quoted Legal Analysis of the Patent Office is relevant and should be followed by the Examiner as controlling. The applicants are not believed to be required to "identify any inconsistency between... guidelines and [the Examiner's §101] rejection" as suggested by the previous Examiner.

> Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility. Ziegler did not even assert that the polypropylene was useful in applications where any of the solid plastics were used. Rather, Ziegler said the polypropylene was "plastic-like."

Id. at 1203, 26 USPQ2d at 1605. Thus, the failure of the applicant to either identify any use for the invention or to disclose features of the invention that would make uses of it readily apparent, was found to render the claimed invention deficient under § 101." Id.

Moreover, the Patent Office has appreciated that

> "Practical considerations require the Office to rely on the inventor's understanding of his or her invention in determining whether and in what regard an invention is believed to be "useful"...
> Courts have repeatedly found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an "immediate benefit to the public" and thus satisfies the utility requirement. As the CCPA held in Nelson v. Bowler:
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> > Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility. [206 USPQ at 883.]

> Similarly, courts have found utility for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition. Accordingly, Office personal should not construe § 101, under the logic of "practical" utility or otherwise, to require that an applicant demonstrate that a therapeutic agent based on a claimed invention is a safe or fully effective drug for humans.
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> These general principles are equally applicable to situations where an applicant has claimed a process for treating a human or animal disorder. In such cases, the asserted utility is usually clear--the invention is asserted to be useful in treating the particular disorder. If the asserted utility is credible, there is no basis to challenge such a claim on the basis that it lacks utility under § 101." [Footnote references omitted.] Id, at pp. 4-5.

The footnotes of the Patent Office's Legal Analysis are instructive in providing a summary of the courts' requirements and are reproduced in the following for the Examiner convenience.

> "[23] The utility being asserted in Nelson related to the a compound with "pharmacological" utility. Nelson, 626 F.2d at 856, 206 USPQ at 883. Office personal should rely on Nelson and other cased as providing general guidance when evaluating the utility of an invention that is based on any therapeutic, prophylactic, or pharmacological activities of that invention.
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> In Nelson v. Bowler, the CCPA addressed the practical utility requirement in the context of an interference proceeding. Bowler challenged the patentability of the invention claimed by Nelson on the basis that Nelson had failed to sufficiently and persuasively disclose in his application a practical utility for the invention. Nelson had developed and claimed a class of synthetic prostaglandins modeled on naturally occurring prostaglandins. Naturally occurring prostaglandins are bioactive compounds that, at the

time of Nelson's application, had a recognized value in pharmacology (e.g., the stimulation of uterine smooth muscle which resulted in labor induction or abortion, the ability to raise or lower blood pressure, etc.). To support the utility he identified in his disclosure, Nelson included in his application the results of tests demonstrating the bioactivity of his new substituted prostaglandins relative to the bioactivity of naturally occurring protaglandins. The Court concluded that Nelson had satisfied the practical utility requirement in identifying the synthetic prostaglandins as pharmacologically active compounds. In reaching this conclusion, the court considered and rejected arguments advanced by Bowler that attacked the evidentiary basis for Nelson's assertions that the compounds were pharmacologically active.

In In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980), an inventor claimed protection for pharmaceutical compounds for treating leukemia. The active ingredient in the compositions was a structural analog to a known anti-cancer agent. The applicant provided evidence showing that the claimed analogs had the same general pharmaceutical activity as the known anti-cancer agents. The Court reversed the Board's finding that the asserted pharmaceutical utility was "incredible," pointing to the evidence that showed the relevant pharmacological activity.

In Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), the Federal Circuit affirmed a finding by the Board of Patent Appeals and Interferences that a pharmacological utility had been disclosed in the application of one party to an interference proceeding. The invention that was the subject of the interference count was a chemical compound used for treating blood disorders. Cross had challenged the evidence in Iizuka's specification that supported the claimed utility. However, the Federal Circuit relied extensively on Nelson v. Bowler in finding that Iizuka's application had sufficiently disclosed a pharmacological utility for the compounds. It distinguished the case from cases where only a generalized "nebulous" expression, such as "biological properties," had been disclosed in a

> specification. Such statements, the court held, "convey little explicit indication regarding the utility of a compound," 753 F.2d at 1048, 224 USPQ 745 (citing In re Kirk, 376, F.2d 936, 941, 153 USPQ 48, 52 (CCPA 1967))."

The applicants note that the present application describes a number of useful products of the disclosed invention, as required by the courts. Similarly, the present application identifies substantial and specific utilities of the presently claimed invention, i.e., methods and treatment of male infertility, such as when caused by protein metabolism disturbances in the epididymis, and compounds and compositions to perform these methods. See, for example, page 4, lines 12-15; page 12, lines 20-25; page 13, lines 3-4; page 13, lines 6-18; page 14, lines 11-14; page 14, lines 22-26; page 14, lines 28 to page 15, line 7; and page 17, lines 7-9 of the specification.

The identification of a tissue-specific marker is a specific or substantial utility worthy of patent protection. The applicants note the CCPA's statements in Nelson, quoted above with approval by the Commissioner of Patents. That is, the new detection capability provided by such tissue-specific reagents which are related to the disorder of male infertility, provides the medical profession with the opportunity to more quickly combat illness and/or alleviate symptoms of such a disorder. Moreover, the applicants note that the present specification identifies more than such a diagnostic utility, as described above.

As a demonstration of the utility of the presently disclosed invention, the Examiner is requested to see the experiments described in the attached Declaration which demonstrate a utility of a receptor protein designated HE6, and of antibodies

against this protein. The receptor protein HE6 has the amino acid sequence shown in SEQ ID NO:2 of the present application.

The attached Declaration of Dr. Gottwald clearly demonstrates that the protein referred to as HE-6 in the present application is a protein with biological significance. The Declaration demonstrates that knocking out the HE-6 gene results in infertility of mice. One of ordinary skill in the art will appreciate from the attached and the present specification that the claimed invention, as represented by HE-6, is biologically significant and useful and that the utility is a result of the biological effects or significance.

Since HE-6 at least contributes to fertility of mice, the protein can be used to screen for substances suitable for male contraception. Screening for agonists can be carried out even if the natural ligand of a protein is unknown. This is shown for example for G-protein linked receptors (see publications of Chen et al., of record). As is clearly stated in the introduction of these publications the effect of over expression of the receptors was already known prior to 1998.

Based on the knowledge of the present application (sequence of the HE-6 DNA and protein) and the common generally advanced knowledge of one of ordinary skill in the art, one of ordinary skill in the art would have been capable of, for example, producing an over expressing cell and using it for screening for agonists.

Further, the protein of the above application can be used for diagnosis of infertility of humans. Since absence of HE-6 results in infertility, the protein is useful for identification of infertility based on expression of HE-6 or the absence thereof. A

respective test could, for example, immunologically detect HE-6 on sperm cells. An example of a respective detection assay is enclosed as a summary of experiments generated by the present applicant (presentation titled "HE-6 expression on sperm surfaces spermatozoa collected from caudal epididymis").

For completeness, the applicants again submit the "derivatives"' of the present claims are sufficiently described by the present disclosure, as noted by the previous Examiner in an Office Action dated July 18, 2001 issued in the co-pending application Serial No. 09/629,437 (Paper No. 5). See, page 7, lines 10-15 of Paper No. 5 issued in the co-pending application.

The comments noted by the previous Examiner in the applicants' publication (DNA and Cell Biol 16(4) 379-389 Apr 1997) are not evidence of a lack of a disclosed utility of the present application. The Examiner must appreciate that the cited publication discloses a utility while appreciating that further work, such as a reasonable amount of experimentation, may always be required or even "essential." Moreover, reference to passages in the applicants' journal article fail to enlighten the analysis of the present disclosure, which describes a number of practical utilities for the disclosed and claimed invention. Accordingly, the claimed invention is submitted to be useful.

The Examiner is requested to see the attached Legal Analysis, specifically at pages 4-5 as well as the footnotes cited therein with regard to the enablement requirement.

The Examiner is requested to return initialed copy of the attached PTO-1449 Form, which include references of record from the parent applications, pursuant to MPEP §609.

Consideration of the attached copy of the Declaration of Dr. Ulrich Gottwald, the original of which was submitted in the noted co-pending application, is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to issue a written restriction requirement in the event the same is believed necessary and/or appropriate.

A separate Request to use the computer readable copy of the Sequence Listing from the parent application is attached.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: _____

**B. J. Sadoff**
Reg. No. **36,663**

**BJS**
1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100